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EXAMINER

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Please find below and/or attached an Office communication concerning this application or proceeding.

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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/072,036
Filing Date: February 05, 2002
Appellant(s): THASTRUP ET AL.

J. Benns
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 9/30/2009 appealing from the Office action mailed 2/19/2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

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(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the supplemental brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Htun, H. et al., "Visualization of glucocorticoid receptor translocation and intranuclear organization in living cells with a green fluorescent protein chimera", PNAS, Vol. 93: pp. 4845-4850.

Carey, K. et al., "Evidence using Green Fluorescent Protein-Glucocorticoid Receptor Chimera that the RNA/TC4 GTPase Mediates an Essential Function Independent of Nuclear Protein Import", J. Cell Biol., June 1996, Vol. 133: pp. 985-996.

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Agarwal, M., "The Antigluco-corticoid Action of Mifepristone", 1996, Pharmacol. Ther., Vol. 70: pp. 183-213.

5,874,231	Sonenberg	2-1999
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5,989,8335	Dunlay	11-1999
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US 20030082564 A1	Thastrup	2003
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Cormack, B. et al., "FACS-optimized mutants of the green fluorescent protein (GFP)", 1996, Gene, Vol. 173: pp. 33-38.

Bar, M. "Visual objects in context", 2004, Nat. Rev. Neuroscience, Vol. 5: pp. 617-629

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 44-52, 73, 77-80 and 82 are rejected under 35 U.S.C. 102(b) as being anticipated by Htun et al (PNAS, 1996, cited by applicants, IDS of 2/5/2002) as evidenced by Carey et al (1996, of record) or Agarwal (Pharmacol. Ther., 1996). **This rejection is maintained for**

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reasons made of record in the Office Actions dated 12/31/2007, 2/19/2009, and for reasons set forth below.

Htun et al disclose a fusion protein of glucocorticoid receptor and GFP (GR-GFP) that was transfected into murine 1471.1 cells that were treated with dexamethasone, RU486, progesterone, or 17 β -estradiol in order to determine the effects of these compounds on the translocation of the GR-GFP fusion protein from the cytoplasm into the nucleus (see the abstract, Figs. 1-3 and 5, and page 4847, second column, third full ¶). The measurement of translocation was done by determining a "variation" of GR-GFP location (either cytoplasmic or nucleic) using time-lapse video microscopy and quantitated by recording microscopic images followed by analysis of the images with custom software from G.W. Hannaway & Associates (see section entitled "Image Acquisition and Analysis", first column, page 4846). The collection of steroid hormones (e.g. dexamethasone, progesterone, etc.) tested by Htun et al is considered to be a "library of compounds", and the methods of Htun et al cited above are considered "screening a library of compounds" according to the arguments set forth in the Ireland Declaration dated 3/20/2007.

Carey et al teach that GR-GFP (or wild type GR) inherently binds the Ran/TC4 GTPase (Ran). Dominant negative mutants of the enzyme Ran were used to identify wild-type Ran as responsible for nuclear import of the GR-GFP protein (see abstract, paragraph bridging first and second columns page 986, and last paragraph, first column, page 994 of Carey et al). Thus, Ran/GR-GFP is a component of the glucocorticoid receptor signaling pathway, with Ran and GR-GFP being subunits of the component. Furthermore, Agarwal teaches that GR inherently binds heat shock proteins in the cytoplasm (¶ linking first and second columns, page 186 and

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Fig. 1). Thus, heat shock protein(s)/GR is a component of the glucocorticoid receptor signaling pathway, with heat shock protein(s) and GR being subunits of the component.

Regarding the amendments to the independent claims 44-46 dated 3/27/2008, these appear almost semantic in nature given the previous claim language and the teachings of the prior art. "Screening" a library of compounds necessarily comprises "determining" whether or not a given library member has a function or effect. Otherwise, why else perform the screening if nothing is to be "determined"? For reasons set forth in the previous Office Action, Htun et al clearly "determined" (i.e. "ascertained" according to applicants definition of "determine", page 11 of the response dated 3/27/2008) that GR-GFP was or was not translocated in response to several steroid library members. This is all that is required to meet the claim step (c) in, for instance, claim 44.

Regarding claims 73 and 80, the term "automated image acquisition" is not defined (or even recited) in the specification. Applicants point to ¶ [0034] for support of "automated image acquisition", however, this ¶ broadly states that the "apparatus system" is automated. Thus, the term "automated image acquisition" is broadly interpreted to include literally any involvement of a computer or electronic system to "automate" image acquisition. See also ¶ [0033] of the published application, in particular the last three lines. In Fig. 5 of Htun et al, it is taught that digital images are imported and manipulated in a computer, which computer then used ANALYZE software to "acquire" a three dimensional image.

Regarding claim 77, Htun et al teach the selection of cells expressing GR-GFP by the use of magnetic beads and amounts of luciferase and CAT activity. See page 4846, first column,

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first full ¶ and the second column, last ¶ to page 4847. Absent a limiting definition of "stable" transformation in the specification, the expression of GR-GFP for the time periods needed for the experiments of Htun et al is considered "stable."

Regarding claims 78 and 79, it has been explained that GR-GFP fusion protein is a subunit of a protein complex. Furthermore, the specification does not provide a definition of the term "substantially the entire protein", thus the term is given a broad interpretation to include the GR-GFP fusion protein as a subunit of the receptor/steroid component of the signaling pathway. GR inherently binds steroid ligands, such as those used by Htun et al for reasons of record.

Regarding claim 82, the specification provides no limiting definition of "spatial frequency method", "object finding" or "object classification." A "spatial frequency" analysis of digital images is considered to be the measurement of how often a structure repeats itself per unit of distance (Bar, 2004). Using such information for the GR-GFP fluorescent signals, it is considered Htun et al "found" or "classified" GR-GFP (an "object") in the digital images of, at least, Figs. 4 and 5. Fig. 5 represents multiple images rendered to form three-dimensional models of cell nuclei containing the GR-GFP, with GR-GFP measured across a given distance, i.e. 30 μm .

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 44-52, 73-80 and 82 are rejected under 35 U.S.C. 103(a) as being unpatentable over Htun et al (PNAS, 1996, of record) as evidenced by Carey et al (1996, of record) in view of Agarwal (of record, 1996), Sonenberg et al (5,874,231, of record) and Dunlay et al (U.S. 5,989,835, e.f.d. 2/27/1997). **This rejection is maintained for reasons made of record in the Office Actions dated 12/31/2007, 2/19/2009, and for reasons set forth below.**

The teachings of Htun et al, Carey et al, and Agarwal et al are set forth above and applied as before. In one interpretation, the set of steroid hormones used by Htun et al would not constitute a "library of compounds" due to the number of compounds used by Htun et al, i.e. four distinct steroid hormones. Thus, one of skill in the art might consider a "library of compounds" to necessarily comprise more than four distinct compounds, although the instant specification and the Ireland Declaration are silent as to how many compounds must be included in order to teach a "library of compounds." Htun et al further teach that their methods of using the GR-GFP fusion protein to study GR receptor translocation and function are a powerful and useful approach to solving several problems in hormone receptor biology (page 4845, first and second columns), and yield distinct nuclear localization results for different receptor ligands (e.g. Fig. 5, dexamethasone vs. RU486). In summary, Htun et al indicate their method is an invaluable tool for further studies of many aspects of hormone receptor biology (page 4850, first column, fourth full ¶).

Agarwal teaches that many glucocorticoid antagonists (i.e. GR receptor antagonists) were well known at the time of the instant invention, and of the desirability of antiglucocorticoids,

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such as RU486, for use in the therapy of a number of diseases. See in particular Figure 2; page 188, second column; and page 199, second column, third full ¶ to page 200.

Sonenberg et al teach methods for screening compound libraries for ligands of steroid receptors in order to identify agents (or lead agents) potentially useful in the treatment of hormone disorders. See in particular the abstract and column 24, line 35 to column 25, line 27.

Regarding the amendments to the independent claims 44-46 dated 3/27/2008, these appear almost semantic in nature given the previous claim language and the teachings of the prior art. "Screening" a library of compounds necessarily comprises "determining" whether or not a given library member has a function or effect. Otherwise, why else perform the screening if nothing is to be "determined?" For reasons set forth in the previous Office Action, Htun et al clearly "determined" (i.e. "ascertained" according to applicants definition of "determine", page 11 of the response dated 3/27/2008) that GR-GFP was or was not translocated in response to several steroid library members. This is all that is required to meet the claim step (c) in, for instance, claim 44.

Regarding claims 73 and 80, the term "automated image acquisition" is not defined (or even recited) in the specification. Applicants point to ¶ [0034] for support of "automated image acquisition", however, this ¶ broadly states that the "apparatus system" is automated. Thus, the term "automated image acquisition" is broadly interpreted to include literally any involvement of a computer or electronic system to "automate" image acquisition. See also ¶ [0033] of the published application, in particular the last three lines. In Fig. 5 of Htun et al, it is taught that digital images are imported and manipulated in a computer, which computer then used ANALYZE software to "acquire" a three dimensional image. Furthermore, Dunlay et al teach

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the automated acquisition of digital images from large numbers of wells comprising fluorescently labeled reporter molecules. See the abstract, col. 3, line 8 to col. 8 and the correlating figures. One such application is scanning for translocation from the cytoplasm to the nucleus (col. 7, lines 47-63).

Regarding claims 74 -76, neither Htun, Agarwal nor Sonenberg et al teach fixation of cells, and Carey et al teach fixation for immunostaining. Neither Htun, Agarwal nor Sonenberg et al reasonably teach the use of well plates for the incubation of cells with compounds of the library. Carey et al teaches 2-well slides for this purpose (page 986, second column, third full ¶).

Dunlay et al teach the fixation of cells for their automated methods of screening. See Example 1 and the passages cited above.

Regarding claim 75, the term "well plate" is not defined in the specification. All that is found in the passage that applicant indicate (¶ [0131]) provides support for this term are the use of 96 well plates. Thus, the term "well plate" is given a broad interpretation to include any tissue culture plate or device that comprises a well. Dunlay et al teach the use of 96 or 384 well plates in, at least, the abstract. Also see Dunlay et al Example 1 wherein incubations with agonists or antagonists are done in the 96 well plates.

Regarding claim 82, for reasons set forth above, "spatial frequency" is considered to be the measurement of how often a structure repeats itself per unit of distance (Bar, 2004). Dunlay et al teach that their methods may also be used to measure the spatial frequency, or distribution, in fluorescently labeled cells (col. 2, first ¶). Such information is more specifically used in an automated fashion by software to find or classify objects such as nuclei. See col. 5, line 55 to col. 8, in particular col. 7, lines 11-20.

The methods of the independent claims are essentially disclosed by Htun et al, with the exception that a "library of compounds" may be interpreted to be larger in number than the four steroid hormones used by Htun et al. The ordinary skilled artisan, seeking methods to study the biology of the GR receptor, or to identify agents with antiglucocorticoid activity, would have been motivated to use the compound libraries taught by Sonenberg et al with the methods of Htun et al because Htun et al teaches their method to be useful and efficient in characterizing the translocation and activity of the GR receptor in response to agonists and antagonists. It would have been obvious for the skilled artisan to do this because of the known benefit of studying the GR receptor response to such agents, as taught by Htun et al; or, alternatively, in order to identify useful antiglucocorticoid agents, as taught by Agarwal et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

The methods of certain dependent claims are essentially disclosed by Htun, Agarwal and Sonenberg et al, with the exception of using fixed cells and multi-well plates. The ordinary skilled artisan, seeking methods to study the biology of the GR receptor, or to identify agents with antiglucocorticoid activity, would have been motivated to use the methods taught by Htun, Agarwal and Sonenberg et al with the methods of Dunlay et al because Dunlay et al teaches their method to be useful and efficient in screening large numbers of compounds for an effect upon fluorescently labeled cells (e.g. GFP reporter molecules or fusion proteins, col. 4 lines 23 - 29), which may include translocation to the nucleus. It would have been obvious for the skilled

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artisan to do this because of the known benefit of maximizing efficiency of experiments when screening large numbers of compounds, as taught by Dunlay et al (e.g. col. 1, lines 9 - 30).

Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 53 and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Htun et al, Carey et al, Agarwal, Sonenberg et al and Dunlay et al as applied to claims 44-52, 73-80 and 82 above, and further in view of Cormack et al (Gene, 1996, of record). **This rejection is maintained for reasons made of record in the Office Action dated 12/31/2007, 2/19/2009, and for reasons set forth below.**

The teachings of Htun, Carey, Agarwal, Dunlay and Sonenberg et al are described above and applied as before. None of these references teach the use of GFP with an F64L mutation.

Cormack et al teach mutations of GFP, including the F64L and S65T (Table 1) substitutions in GFPmut1, which had a 35-fold increase in fluorescence intensity relative to wt GFP (Table II, page 37). Cormack et al teach these GFP mutants to have wide applicability in any GFP study (page 38, first column, number (4)), that they fluoresce more intensely, and are more stable due to efficient folding (abstract and paragraph linking pages 33 and 34).

The claimed methods are essentially disclosed by Htun I, Carey, Agarwal, Dunlay and Sonenberg et al with the exception of the GFP F64L substitution. The ordinary skilled artisan,

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seeking a method to detect translocation of GFP-tagged proteins would have been motivated to use GFP F64L/S65T substitution (or the other GFP mutants) with the detection methods of Htun et al because Cormack et al teaches them to be well known types of GFP proteins that have utility for detection in cell culture and to have superior fluorescence and stability properties. It would have been obvious for the skilled artisan to do this because of the known benefit of using a GFP protein with superior fluorescence and stability as taught by Cormack et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 48 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons made of record in the Office Action dated

5/30/2007, 12/31/2007, 2/19/2009, and for reasons set forth below.

Claim 48 (amended 3/20/2007) recites a "synthetic chemical compound". The response does not indicate specifically where in the specification support may be found for the limitation, which is intended to be a narrowing limitation of the compounds recited in the base claims 44-46 (see page 12 of the response dated 3/20/2007). A review of the specification does not reveal any support for "synthetic chemical compounds" as a narrowing limitation of the library of compounds recited in the base claims. In fact, a search of the specification does not reveal use of the word "synthetic." Therefore, there is no support for the limitation "synthetic chemical compound." Thus, the amended claim includes impermissible New Matter.

(10) Response to Argument

Applicant's arguments filed 9/30/2009 have been fully considered but they are not persuasive.

The 35 USC 102(b) rejection over Htun et al

Applicants essentially assert that: 1) Carey et al does not teach that Ran binds to GR, thus, Ran/GR is not to be considered a "component of an intracellular pathway"; 2) GR does not have the biological activity of the Ran/GR complex; 3) GR does not exhibit an activity of the HSP/GR complex, which does not translocate as part of an intracellular pathway; 4) Htun et al does not teach screening a library of compounds because the effect of the compounds of Htun et al on GR were already known; 5) Htun et al does not teach the limitations of claim 46 because GR is a complete, biologically functional protein, which is excluded by claim 46; 6) Htun et al do not teach the step of claim 73; 7) Htun et al does not teach the use of stably transformed cells; 8) Htun et al do not teach any of the recited spatial frequency methods in claim 82.

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Regarding 1), this is a limited view of the teachings of Carey et al and does not take into account the entire reference, or even the section cited by applicants. Reading the section further, Carey et al teach that Ran does effect GR directly: "...the observed inhibition of GR-GFP translocation by Ran mutants is a direct effect on nuclear transport, rather than a long-term, indirect response." See page 990, second column, last ¶ in particular. The entire reference is also positive towards the Ran/GR interaction. See the Introduction beginning on page 985 teaching the involvement of Ran in the nuclear import of proteins having a nuclear localization signal, or NLS, and that GR possesses two NLSs.

Regarding 2) and 3), this line of reasoning is less than clear. When bound to Ran, GR has, *inter alia*, the activity of being translocated to the nucleus, thus meeting the claim limitation. In light of the broad language used in the claims and the lack of any limiting definition in the specification of either a "subunit", a "component of an intracellular pathway", or a "biological activity of the component", the corresponding phrase has been given a broad interpretation to include any given, arbitrary activity of the component. Such activities include the ability of GR to bind a ligand, to translocate to the nucleus from the cytoplasm, and to initiate transcription once in the nucleus. According to Carey et al, GR exhibits the translocation activity when bound to Ran. The totality of the prior art (i.e. Carey, Agarwal) further suggests GR can bind ligand or initiate transcription when not bound to Ran. Furthermore, the choice of what makes up the component in this case is also arbitrary as long as it interacts with GR in some fashion at some point in an intracellular pathway. The Examiner has provided evidence that GR also binds heat shock proteins, and it also binds proteins involved in transcription once in the nucleus (e.g. Htun et al teach localization of GR-GFP on target genes in the nucleus, also see Agarwal). Any of

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these could be, and are, considered other "subunits" that together comprise "components" of an intracellular pathway. A reading of the claims does not reveal that the component must be translocated, as applicants appear to insist. What is actually recited is that the subunit is assayed for translocation (see, e.g. step (c) in claim 44). In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., assaying translocation of a component) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Finally, as explained in previous Office Actions, the problem is that a "component", even if treated as a "fully functional protein", can still be considered a subunit. This is because "fully functional proteins" involved in intracellular pathways bind to and modify other "fully functional proteins", the complex of said "fully functional proteins" being a "component" of the pathway and the individual proteins "subunits." One example is the NF- κ B and I κ B proteins listed in the instant specification as examples of components of intracellular pathways. These proteins bind to form a multimeric complex in the cytoplasm of cells, in which case NF- κ B and I κ B are each considered subunits of said complex. Thus, they meet the definition of a subunit, and seemingly also meet applicants' definition of a "fully functional protein", i.e. a component.

Regarding 4), in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., using only compounds with unknown effects on the subunit) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the

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specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, the definition of screening provided in the Ireland declaration amounts to an opinion for reasons of record. Such opinion is generally not probative when unsupported by facts or evidence, see MPEP §716.01(c). It is reiterated that the effects of the compounds used by Htun et al were not known with respect to translocation the GR-GFP protein, i.e. the subunit encompassed by the claims. Nor were the differential effects of the compounds on the three-dimensional localization of GR or GR-GFP in the nucleus known until Htun et al did the experiments (e.g. the results presented in Fig. 5 of Htun et al). Either situation is considered a teaching of "screening" compounds for extensive reasons made of record and reiterated above.

Regarding 5), in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the subunit of claim 46 is not a complete, biologically active protein; that there are no peptide linkages between the subunits) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Furthermore, the claim language does not rule out either the GR/Ran complex, the GR/HSP complex, or the complex of GR with the proteins involved in transcription of target genes as these are all "polypeptides." It is noted the relevant examples in the instant specification teach much the same, i.e. the subunits of the PKA proteins are not disclosed as being linked by inter-protein peptide bonds (e.g. disulfide bridges, as the regulatory subunits of PKA are released from the catalytic core upon binding of ligand, ¶ [0009] of the published

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application, US 20030082564 A1). Finally, it is noted that the instant specification teaches that transcription factors that change localization upon activation (e.g. GR) are considered an aspect of the claimed invention (¶ [0043]).

Regarding 6), Htun et al teaches obtaining images using an automated apparatus for reason of record despite applicants protests to the contrary. See, again, page 4846, first column, second and third full ¶. A computer workstation connected to a fluorescent microscope and a scanning unit was used by Htun et al to capture images: these are all components of the system disclosed in applicants own specification as just such an "automated apparatus" (e.g. see ¶'s [0033] - [0035] as referred to by applicants on page 15 of the appeal brief). A review of the relevant sections of Htun et al does not reveal the word "manual" or "manually" as applicants assert. Finally, it is noted that the term "automated image acquisition" is not defined (or even recited) in the specification. Thus, the term "automated image acquisition" is broadly interpreted to include literally any involvement of a computer or electronic system to "automate" image acquisition.

Regarding 7), Htun et al teach the selection of cells expressing GR-GFP by the use of magnetic beads and amounts of luciferase and CAT activity. See page 4846, first column, first full ¶ and the second column, last ¶ to page 4847. Absent a limiting definition of "stable" transformation in the specification, the expression of GR-GFP for the time periods needed for the experiments of Htun et al is considered "stable." That Htun et al initially transiently transfected certain cells is not in dispute, but the subsequent selection of such cells for expression of the desired transgenes as set forth above is a common step for providing stable expression. See applicants own example of the selection of cells that were initially transiently transfected (¶'s

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[0151], [0190]). Based upon the successful results of Htun et al in screening compounds for the ability to induce GR-GFP translocation, this is considered to be "stable expression" adequate for screening. In the ¶ bridging the first and second columns of page 4847 through the second column of Htun et al, it is taught that all of the cells that express GR-GFP were functional in response to dexamethasone. This was more than adequate for Htun et al to determine the effects of the compound library on GR-GFP, and again is an indicator of stable expression, not transient expression (which often does not produce expression in such a high percentage of cells without selection).

Regarding 8), applicants are directed to page 5 of the final Office Action dated 2/19/2009 wherein it was explained that Htun et al are considered to have taught "object finding" and "object classification", at the least. This is because the specification provides no limiting definition of "spatial frequency method", "object finding" or "object classification." A "spatial frequency" analysis of digital images is considered to be the measurement of how often a structure repeats itself per unit of distance (Bar, 2004). Using such information for the GR-GFP fluorescent signals, it is considered Htun et al "found" or "classified" GR-GFP (an "object") in the digital images of, at least, Figs. 4 and 5. Fig. 5 represents multiple images rendered to form three-dimensional models of cell nuclei containing the GR-GFP, with GF-GFP measured across a given distance, i.e. 30 μm .

The 35 USC 103(a) rejection over Htun, Carey, Agarwal, Sonenberg and Dunlay et al

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Applicants essentially assert that: 1) Htun and Carey et al are deficient for the reasons set forth above; 2) none of the references teaches the limitations of claim 46 because GR is a complete, biologically functional protein, which is excluded by claim 46

Regarding 1), this is unconvincing for the reasons set forth above in the response to arguments against the 35 USC 102(b) rejection.

Regarding 2), this assertion is also addressed above in the arguments against the 35 USC 102(b) rejection, see section 5).

The 35 USC 103(a) rejection over Htun, Carey, Agarwal, Sonenberg and Dunlay et al in further view of Cormack et al

Applicants essentially assert that: 1) Htun and Carey et al are deficient for the reasons set forth above; 2) none of the references teaches the limitations of claim 46 because GR is a complete, biologically functional protein, which is excluded by claim 46.

Regarding 1), this is unconvincing for the reasons set forth above in the response to arguments against the 35 USC 102(b) rejection.

Regarding 2), this assertion is also addressed above in the arguments against the 35 USC 102(b) rejection, see section 5).

The 35 USC 112 1st ¶ written description rejection

Applicants essentially assert that taken together, the disclosures of certain paragraphs in the published US application provide support for claim 48.

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This assertion is not convincing. Claim 48 is intended to be further limiting of claims 44-46, which all recite the use of a "library of compounds." As has been explained (Office Actions of 12/1/2005, 10/20/2006, 5/30/2007) the disclosure of "chemical substances" has little bearing on using a "library of compounds", which, as set forth in the Ireland Declaration, implies a level of purity and availability of the compounds: a level not encompassed by or required for the term "chemical substances." The term "synthetic compounds" is much broader than the "organic compounds" that are to be synthesized in ¶ [0118]. Organic compounds are a broad class of compounds comprising carbon, whereas inorganic compounds are those broadly classified to be of mineral origin. Both organic and inorganic compounds are considered to be included in the genus of "synthetic compounds" : e.g. common salts are synthetic compounds (e.g. Rochelle salt synthesis) but most, if not all, are not organic compounds. Thus, a teaching of synthesizing organic compounds cannot provide support for the broad genus of synthetic compounds.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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